UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	MDL Docket No. 2738
This Document Relates To All Cases	

DEFENDANTS JOHNSON & JOHNSON AND JOHNSON & JOHNSON CONSUMER INC.'S MEMORANDUM OF LAW IN OPPOSITION TO PLAINTIFFS' STEERING COMMITTEE'S MOTION TO EXCLUDE THE OPINIONS AND TESTIMONY OF DEFENDANTS' EXPERTS DR. CHERYL SAENZ AND DR. KEVIN HOLCOMB

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INTRODUCTION

Drs. Cheryl Saenz and Kevin Holcomb are highly-regarded and exceedingly well-credentialed physicians who specialize in the practice of gynecological oncology, i.e., the diagnosis and treatment of women with ovarian and other gynecological cancers.[1] Both experts have significant clinical and research experience, each having treated hundreds of patients for reproductive cancers throughout his/her career and published on issues relating to the detection of ovarian cancers.[2]

Despite these experts' significant experience and knowledge in the area of gynecological oncology – and, more specifically, what is scientifically known about the origins of and risk factors for ovarian cancers – plaintiffs argue that they should be barred from providing testimony on the issue of general causation. Plaintiffs' arguments lack merit and should be rejected.[3]

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1 (*See* Expert Report of Cheryl Christine Saenz, M.D. ("Saenz Rep.") at 1, Feb. 25, 2019 (attached as Ex. C12 to the Omnibus Certification of Julie L. Tersigni, May 7, 2019 (ECF No. 9723-2)); Expert Report of Kevin Holcomb, M.D., FACOG ("Holcomb Rep.") at 1, Feb. 25, 2019 (attached as Ex. C27 to Tersigni Cert.).)

2 (*See* Saenz Rep. at 2; Holcomb Rep. at 2.)

3 While plaintiffs' motion is styled as one to exclude the opinions of Drs. Holcomb and Saenz in their entirety, significant portions of their reports are untouched by plaintiffs' criticisms. For example, Drs. Holcomb and Saenz each provide a detailed background regarding the various subtypes of ovarian cancers, their established risk factors, characteristics that are associated with a reduction in

First, contrary to plaintiffs' suggestion, Drs. Saenz and Holcomb's general causation opinions are based on a reliable methodology that considers the totality of the scientific evidence.

Second, plaintiffs' accusation that Drs. Saenz and Holcomb applied an improper "certainty"[4] standard to the biological plausibility factor of the Bradford Hill framework is false. Rather, the gist of these experts' opinions is that biological plausibility means something more than an untested hypothesis or one that is unsupported by any reliable science.

Third, there is no merit to plaintiffs' argument that Dr. Saenz requires a degree in epidemiology to criticize opinions offered by their epidemiology expert, Rebecca Smith-Bindman. Courts have repeatedly held that physicians, such as Dr. Saenz, who have relevant clinical and research expertise, are fully qualified to opine on epidemiological issues. And despite plaintiffs' assertion to the contrary, Dr. Saenz's critiques of Dr. Smith-Bindman for relying on incorrect data in her report are well-supported by the facts in the record.

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risk and specific criticisms of particular opinions offered by certain plaintiffs' experts. (*See* Saenz Rep. at 3-8, 22-30; Holcomb Rep. at 4-7, 19-23.)

[4] (Pls.' Steering Committee's Mem. of Law in Supp. of its Mot. to Exclude the Ops. & Test. of Defs.' Gynecology-Oncology Experts Dr. Cheryl Saenz & Dr. Kevin Holcomb ("Pls.' Br.") at 2, 31, May 7, 2019 (ECF No. 9735-1).)

For all of these reasons, discussed in more detail below, plaintiffs' motion to exclude the opinions of Drs. Holcomb and Saenz should be denied.

BACKGROUND

A. Dr. Saenz

Dr. Saenz is a Clinical Professor of Gynecologic Oncology in the Department of Obstetrics, Gynecology and Reproductive Sciences at the University of California, San Diego. She has a B.A. in Biopsychology from Cornell University and an M.D. from the University of California, Irvine College of Medicine, and is board-certified in the areas of Obstetrics and Gynecology and Gynecologic Oncology by the American Board of Obstetrics and Gynecology.[5] Her responsibilities in her current position as an educator include teaching fellows, residents and medical students about all aspects of gynecologic malignancies, including epidemiology, risk factors for development, histopathology and pathophysiology, prevention, diagnosis and treatment of gynecologic cancers.[6] In addition to her work as a professor, Dr. Saenz also has more than 20 years of experience as an attending physician at UC San Diego Health System, where she performs surgical procedures and prescribes chemotherapy and immunotherapy for

[5] (Saenz Rep. at 1-2.)

[6] (*Id.* at 1.)

patients with reproductive cancers.[7] Dr. Saenz is an active researcher in the area of gynecologic oncology, and has published research in numerous journals regarding ovarian, cervical and endometrial cancers.[8] One of her most active areas of investigator-initiated research is the early detection of ovarian cancer.[9] She is a member of several organizations in the areas of gynecology and/or oncology, including the Society of Oncology, and served on the Board of Directors of the Foundation for Women's Cancer from 2007-2013, including as the Chair of the Foundation's Education Committee from 2013-2016.[10] The core opinions provided by Dr. Saenz's report are that: (1) there are well-established risk factors for ovarian cancer and talc is not one of them; and (2) plaintiffs' experts' hypotheses of biologic plausibility are based on pure speculation.

First, Dr. Saenz explains that there are several well-established risk factors that have been associated with a woman having an increased risk of developing ovarian cancer, including the most influential risk factor: inherited mutations in genes that can increase the risk of developing ovarian cancer to as high as 50-60%

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7 (*Id.*)

8 (*Id.* at 2.)

9 (*Id.*)

10 (*Id.*)

over the course of a woman's lifetime.[11] Based on a review of the epidemiologic literature, Dr. Saenz opines that genital application of talc is not a risk factor for the development of ovarian cancer.[12] As Dr. Saenz explains, none of the cohort studies that have been published on this topic – each of which asked large numbers of women questions about their genital use of talc and then followed them to see if they developed ovarian cancer – has demonstrated a statistically significant association between talc and ovarian cancer.[13] And while certain retrospective case-control studies have shown a weak association, these studies suffer from internal discrepancies, contradict one another other, and do not demonstrate a consistent dose-response relationship between talc use and ovarian cancer.[14] Further, Dr. Saenz notes that the case-control studies are generally viewed as less reliable than cohort studies due to inherent selection and recall biases.[15]

Second, Dr. Saenz explains that the scientific evidence does not support plaintiffs' theories of migration and inflammation. As Dr. Saenz notes, plaintiffs' experts' theory of migration relies on a gross mischaracterization of female

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11 (*Id.* at 7.)

12 (*Id.* at 8, 9-17.)

13 (*Id.*at 8, 13-16.)

14 (*Id.* at 8, 9-13.)

15 (*Id.*)

reproductive anatomy, including an inappropriate attempt to conflate the vagina and the perineum and to characterize the female genital tract as an open conduit.[16] In addition, Dr. Saenz notes that plaintiffs' experts' hypothesis that talc causes chronic inflammation, which in turn causes ovarian cancer, is not supported by scientific evidence and contradicts what is known about the origins of ovarian cancer.[17]

B. Dr. Holcomb

Dr. Holcomb is an Associate Professor of Clinical Obstetrics and Gynecology at Weill Medical College of Cornell University.[18] He also serves as the Director of Gynecologic Oncology, Vice-Chairman of Gynecology, and Director of Minimally Invasive Surgery in Weill Cornell's Department of Obstetrics and Gynecology.[19] Dr. Holcomb holds an M.D. from New York Medical College and a B.A. from Cornell University.[20] The majority of Dr. Holcomb's time is spent in clinical practice as a gynecologic oncologist; he has performed approximately 200 to 225 surgeries per year since the early 2000s and

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16 (*Id.* at 17-18, 27-28.)

17 (*Id.* at 8-9, 28-29.)

18 (Holcomb Rep. at 1.)

19 (*Id.*)

20 (Holcomb Rep., Ex. A (curriculum vitae).)

treats approximately 20 new ovarian cancer patients per year.[21] Dr. Holcomb's clinical responsibilities also include assessing cancer risk in his patients through the identification of genetic, reproductive and environmental risk factors.[22]

As part of his duties, Dr. Holcomb reviews pathology slides for every patient on whom he operates for ovarian cancer.[23] In addition, as part of his role on the tumor board for Weill Cornell, he reviews slides of precursor lesions for high grade serous ovarian cancer from women (typically with genetic mutations) who undergo risk-reducing surgery.[24]

Dr. Holcomb has personally authored or co-authored more than 70 peer-reviewed articles, and is currently the principal investigator for two multi-institutional prospective trials examining the role of a biomarker in the early detection of ovarian cancer.[25] Dr. Holcomb acts as a reviewer of research submitted for publication to several journals, including *Gynecologic Oncology*, and makes recommendations regarding the appropriateness and validity of the

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21 (*Id.* at 1.)

22 (*Id.*)

23 (Holcomb Dep. 450:9-16.)

24 (*Id.* 448:18-449:16.)

25 (Holcomb Rep. at 2.)

submitted research based on assessment of the study design, statistical analysis and presentation of the findings.[26]

In his report, Dr. Holcomb opines that there are a variety of known risk factors for the development of the various subtypes of ovarian cancer, including genetic predisposition and reproductive history, use of hormone replacement therapy drugs, and cigarette smoking.[27] By contrast, Dr. Holcomb explains, a review of the available epidemiological evidence leads to the conclusion that genital talc use is not associated with, much less does it cause, an increased risk of ovarian cancer.[28] In addition, Dr. Holcomb notes that plaintiffs' experts' opinions regarding the alleged mechanism by which talc purportedly causes ovarian cancer are not biologically plausible. Specifically, Dr. Holcomb explains that plaintiffs' experts' theory of migration – i.e., that talc particles can ascend the female genital tract – is not supported by the studies on which they rely and is undermined by other scientific evidence.[29] Dr. Holcomb also opines that plaintiffs' experts' theory that talc particles cause chronic inflammation that either initiates or promotes

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26 (*Id.*)

27 (*Id.* at 3, 5-7.)

28 (*Id.*at 9-16.)

29 (*Id.* at 16-17.)

carcinogenesis is similarly contradicted by the existing scientific evidence.[30] For example, studies have shown that the use of talc in a procedure called pleurodesis – which involves the direct injection of talc into the cavity surrounding the lungs to prevent the buildup of air or fluid there – does not increase the risk of cancer among patients and may, in fact, have a protective effect.[31]

ARGUMENT

I. THE OPINIONS OFFERED BY DRS. SAENZ AND HOLCOMB REGARDING THE LACK OF A CAUSAL CONNECTION BETWEEN COSMETIC TALC USE AND OVARIAN CANCER ARE THE PRODUCT OF A RELIABLE METHODOLOGY.

Drs. Saenz and Holcomb have each opined, based on a fulsome review of the relevant epidemiological literature, that the available science does not support the position that exposure to cosmetic talcum powder can cause ovarian cancer. Plaintiffs' efforts to criticize their methodologies should be rejected.

A. Drs. Saenz And Holcomb Reliably Considered The Totality Of The Epidemiological Evidence In Forming Their General Causation Opinions.

Plaintiff first complain that Drs. Saenz and Holcomb's opinions are unreliable because they applied the hierarchy of epidemiologic evidence (which plaintiffs reject), gave more weight to cohort studies than case-control studies and

30 (*Id*. at 3, 17-18.)

31 (*Id*. at 18-19.)

opined that the case-control studies were subject to recall bias. None of these overlapping arguments has any merit.

1. Plaintiffs' Attacks On The Hierarchy Of Evidence Should Be Rejected.

As an initial matter, and as set forth in detail in defendants' General Causation Brief and Epidemiology *Daubert* Opposition,[32] the hierarchy of evidence is a well-established concept that is widely accepted in the scientific community. Plaintiffs argue that Dr. Holcomb's opinions about this hierarchy should be rejected solely because the diagram he used in his report to illustrate this principle came from a non-scientific source.[33] This argument is frivolous. As Dr. Holcomb explained at his deposition, the illustration was merely included in the report to show the "widely held hierarchy on the strengths of different study types based on their ability to be altered by inaccuracies . . . consistent with what [he] already knew" from his medical fellowship coursework.[34] He was not relying on the graphic to inform his opinion. Moreover, plaintiffs' suggestion that Dr.

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32 (*See* Defs.' Mem. of Law in Supp. of Mot. to Exclude Pls.' Experts' General Causation Ops. ("General Causation Br.") at 9-12, May 7, 2019 (ECF No. 9736); Mem. of Law in Opp'n to Pls.' Mot. to Exclude the Ops. of Defs' Epidemiology Experts at 32-36 (filed herewith and incorporated herein).)

33 (Pls.' Br. at 11; *see also* Holcomb Rep. at 8.)

34 (Dep. of Kevin Holcomb, M.D. ("Holcomb Dep.") 281:21-284:15, Mar. 27, 2019 (attached as Ex. C to Pls.' Br.).)

Holcomb's "own institution," Weill-Cornell, does not follow the established hierarchy of scientific evidence[35] is flatly contradicted by the expert report and deposition testimony of Dr. Karla Ballman, Chief of the Division of Biostatistics and Epidemiology at Weill Cornell. Dr. Ballman has opined that generally, "prospective cohort studies yield a higher level of evidence than case-control studies,"[36] she included her own diagram showing as much in her report,[37] and she testified that the greater reliability of cohort studies compared to case-control studies is "a fairly well established principle" in epidemiology.[38] For all of these reasons, plaintiffs' argument that Dr. Holcomb's opinions are unreliable because he applied the hierarchy of evidence in evaluating the available epidemiological evidence should be soundly rejected.

2. Plaintiffs Are Wrong That Drs. Saenz And Holcomb "Ignore" The Case-Control Studies.

Although Drs. Saenz and Holcomb both recognize the hierarchy of evidence, they also both made it crystal clear in their reports and depositions that they considered the totality of the evidence in reaching their conclusions, including both

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35 (Pls.' Br. at 12.)

36 (Expert Report of Karla Ballman, Ph.D. at 7, Feb. 25, 2019 (attached as Ex. C25 to Tersigni Cert.).)

37 (*Id.* at 4.)

38 (Dep. of Karla Ballman, Ph.D. 19:17-24, Mar. 22, 2019 (attached as Ex. B32 to Tersigni Cert.).)

case-control and cohort studies. Plaintiffs nonetheless complain that the two experts' methods are invalid because they "dismissed" or "ignored" the case-control studies.[39] This argument cannot be reconciled with the actual record.

Dr. Saenz. Even a cursory review of Dr. Saenz's report demonstrates that she considered all the relevant epidemiological literature, including the case-control studies, in developing her causation opinions. Indeed, Dr. Saenz's report contains a four-page section titled "Case-Control Studies," as well as a separate, attached table that further analyzes those studies.[40] As Dr. Saenz explains in these portions of her report, while some of the case-control studies show weak associations between ovarian cancer and the perineal application of talc,[41] this cannot establish a causal relationship because, *inter alia*, the results of the case-control studies conflict,[42] the majority of the case-control studies did not find a statistically significant association,[43] many of the case-control studies have internal inconsistencies,[44] the case-control studies generally failed to demonstrate a dose-

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39 (Pls.' Br. at 7, 8, 11, 14.)

40 (Saenz Rep. at 9-13, tbl. 1.)

41 (*See id.*)

42 (*See id.* at 11 (discussing inconsistencies between the population-based and hospital-based studies).)

43 (*See id.* at 9.)

44 (*See id.* at 10.) For example, the Cramer (1999) study reported that 5-20 years of talc use increased the risk of ovarian cancer, but 8-19 years did not. (*Id.*)

response curve,[45] and case-control studies suffer from inherent selection and recall biases that call their reliability into question, particularly where the reported associations are weak.[46] Dr. Saenz's report also includes a separate section analyzing the meta-analyses and pooled analyses, which explains that these studies incorporate the same data as the case-control studies, and therefore are subject to the same limitations, and also failed to demonstrate a consistent dose-response curve.[47] In short, far from dismissing the case-control studies out of hand, Dr. Saenz considered them extensively.

Plaintiffs' argument to the contrary relies on misconstruing and misrepresenting selected portions of Dr. Saenz's deposition testimony. For example, the section of Dr. Saenz's deposition that plaintiffs cite for the proposition that she "based her opinions solely on the reports of the cohort studies in isolation" says nothing of the sort.[48] To the contrary, Dr. Saenz testified that the cohort studies were only "*part* of the data that [she] used to formulate [her]

The Cramer (2016) study reported that fewer than 30 talc applications per month doubled a woman's risk, but 40 or more had no statistically significant impact. (*Id.* at 10-11.) Also, the Wu (2009) study failed to show a statistically significant association for the known ovarian cancer risk factor of family history. (*Id.* at 10.)

45 (*See id.*)

46 (*See id.* at 8, 12-13.)

47 (*See id.* at 16-17.)

48 (Pls.' Br. at 10.)

opinions."[49] Moreover, Dr. Saenz later reasserted that her opinions were based on the totality of the epidemiological data, noting that while the cohort studies "***helped*** form [her] opinion," she reached "the conclusions that [she has] come to, because [she] read ***all*** of" the relevant studies, including the case-control studies and meta-analyses.[50]

Plaintiffs also assert that Dr. Saenz conceded at her deposition that she "did not weigh the totality of the evidence" because she did not evaluate the cohort studies' design limitations.[51] But, in the testimony they cite, Dr. Saenz explains that the authors of the cohort studies "do that themselves in their discussion sections," [52] and a few lines later, she testified that she did consider those limitations in formulating her opinions.[53] Additionally, plaintiffs argue that Dr.

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49 (*Id.* (citing Dep. of Cheryl Saenz, M.D. ("Saenz Dep.") 181:22-182:3, Mar. 13, 2019 (attached as Ex. A to Pls.' Br.)) (emphasis added).)

50 (Saenz Dep. 329:4-330:2 (emphases added); *see also id.* 292:9-13 (Dr. Saenz noting that "[t]he case control studies, I don't have criticism of all of them," but "when I'm reviewing them, I review the data in its entirety, particularly looking for consistencies within the study"); *id.* 341:3-12 (testifying, as to the meta-analyses, "I don't discount them. I absolutely reviewed them and I considered them in my opinion, but I don't think that their findings are anything unique or different. . . . I think the fact that they all report similar odds ratio[s] is not at all surprising, because they're using the same data").)

51 (Pls.' Br. at 10.)

52 (Saenz Dep. 181:9-13 (cited in Pls.' Br. at 10).)

53 (*Id.* 181:14-20.)

Saenz found the epidemiology to be "inconsistent solely because 'the cohort studies do not show an increased risk,'" while the case-control studies do.[54] This is untrue. As set forth above, Dr. Saenz expressly notes inconsistencies among the case-control studies as well.[55] In any event, the divergence between the cohort studies and the case-control studies ***is*** an inconsistency in the data that is relevant to the causation analysis and supports Dr. Saenz's opinions.[56]

There is also no merit to plaintiffs' insistence that, because Dr. Saenz testified that she "wouldn't use the word weigh" to describe how she evaluated the cohort studies versus the case-control studies, she must have failed to value the latter at all.[57] When the testimony is viewed in its proper context, it is clear that Dr. Saenz was only noting that she had not conducted a formal meta-analysis applying a recognized weighting mechanism (e.g., the Newcastle-Ottawa Scale[58]).

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54 (Pls.' Br. at 9 (quoting Saenz Dep. 309:25-310:4).)

55 (Saenz Rep. at 11.)

56 (Saenz Dep. 308:14-309:2.) Dr. Saenz also testified to the additional inconsistency, within the case control studies, between the hospital-based and population-based studies, and to her belief that the hospital-based studies (which have not found a statistically significant association) are superior because they "compar[e] like to like." (*Id.* 344:2-345:8.)

57 (Pls.' Br. at 9 (quoting Saenz Dep. 166:18-167:17).)

58 The Newcastle-Ottawa Scale is a tool used to "assess the quality of non-randomised studies" when performing a formal meta-analysis. *See* Wells et al., *The Newcastle-Ottawa Scale(NOS) for assessing the quality of nonrandomised studies in meta-analyses*, The Ottawa Hospital, http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (last visited May

At no point did she suggest that she failed to consider or account for the case-control studies in her causation analysis.[59]

Dr. Holcomb. Plaintiffs' arguments with respect to Dr. Holcomb are similarly meritless because he, too, considered the totality of the evidence in generating his causation opinions. In his report, Dr. Holcomb, like Dr. Saenz, discusses the case-control studies in a separate section and includes a table delineating the study results,[60] all of which plaintiffs largely ignore. Dr. Holcomb also dedicated a section of his report to the meta-analyses that incorporate the case-control data.[61] In addition, Dr. Holcomb testified repeatedly at his deposition that he reviewed and considered all of the epidemiological data, stating for example: "I looked at the literature in totality. So if you just restrict to the epidemiologic data, I looked at the case-control studies. I spent a fair amount of time going through those, looking for consistency and things like that. And then I looked at the cohort studies . . . ."[62]

23, 2019) (attached as Ex. A173 to Suppl. Certification of Julie L. Tersigni ("Suppl. Tersigni Cert.")).

59 (Saenz Dep. 166:18-167:17.)

60 (Holcomb Rep. at 9-10, tbl. 1.)

61 (*Id.* at 13-15.)

62 (Holcomb Dep. 137:4-18; *see also id.* 48:20-49:6 ("[I]t is the totality of the data that led me to my opinion."); *id.* 307:4-308:5 (testifying that he did not rely primarily on the cohort study in coming to his opinions but rather on "the totality" of the literature, looking at "the whole picture" including the case-control studies).)

Plaintiffs also argue that Dr. Holcomb's review of the literature is invalid because he purportedly "failed to acknowledge or even consider the cohort's design limitations."[63] But Dr. Holcomb explained at his deposition that he ***did*** evaluate the limitations of both the cohort studies and case-control studies in preparing his report.[64] For example, Dr. Holcomb observed that sample size is often a concern with cohort studies, but that after reviewing the relevant literature, he determined that they were sufficiently powered.[65] Thus, Dr. Holcomb explained that while he did evaluate the cohort studies critically, he "was able to put [any of the potential criticisms] to rest with [his] reading of those cohort studies."[66]

Dr. Holcomb also testified that he created his report's Table 1, "a list of case-control studies that [he] reviewed in regard to this matter," both "to show that [he] performed a comprehensive review" and because reviewing the case-control studies was critical to evaluating plaintiffs' experts' claim that the epidemiologic data consistently show an increased risk of ovarian cancer with talc exposure. (*Id.* 148:21-150:11.) Based on his review, Dr. Holcomb not only disagrees with that claim but finds it scientifically indefensible. (*See id.* 157:19-158:17.)

63 (Pls.' Br. at 12.)

64 (Holcomb Dep. 313:14-315:4.)

65 (*See id.* 313:20-314:10.)

66 (*Id.* 314:13-315:4; *see also id.* 352:4-353:11 (Dr. Holcomb explaining that he did not mention a limited latency period as a limitation of a particular cohort study because, given the study's 14-year follow-up time and the high likelihood that study subjects began using talc some time before the study began, he did not view it as a weakness of the study).)

In short, the testimony and reports offered by Drs. Saenz and Holcomb expressly refute plaintiffs' suggestion that these experts "ignored" or "disregarded" the case-control studies in their analyses.

3. Drs. Saenz And Holcomb Assess Recall Bias Properly.

Plaintiffs also make the redundant argument in a separate section of their brief that Drs. Saenz and Holcomb improperly "dismiss all case-control studies based on" recall bias.[67] As set forth above, however, these experts do ***not*** dismiss the case-control studies. Moreover, their analysis of recall bias is reliable and spot-on.

Recall bias is a "systematic error" that can occur in backward-looking (such as case-control) studies whereby study participants' "recall of past exposures or experiences differs between the patients with . . . and those without . . . the specific disease of interest."[68] As explained in the J&J defendants' General Causation Brief, it is well-recognized by the scientific community that recall bias can distort study results.[69] Indeed, multiple studies – including the Langseth (2008) study co-

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67 (Pls.' Br. at 17.)

68 (Holcomb Rep. at 8-9.)

69 (*See* General Causation Br. at 23-25 (citing Schildkraut et al., *Association between Body Powder Use and Ovarian Cancer: The African American Cancer Epidemiology Study*, 25(10) Cancer Epidemiol Biomarkers Prev. 1411, 1416 (2016) ("Schildkraut 2016") (attached as Ex. A129 to Tersigni Cert.)).)

authored by plaintiffs' expert Dr. Siemiatycki, and other studies relied upon by plaintiffs' experts – have identified recall bias as a particular concern in the case-control studies regarding talc and ovarian cancer.[70]

Plaintiffs insist in their briefing that Drs. Saenz and Holcomb "selectively rely on a single study," Schildkraut (2016) – which is also cited by all of plaintiffs' gynecologic oncology experts – "to dismiss all case control studies as being influenced by recall bias."[71] In that case-control study, women with ovarian cancer who were interviewed after 2014 reported markedly higher talc use than those interviewed before 2014 (51.5% versus 36.5%), while reports of talc use for women without ovarian cancer were essentially the same regardless of when they were interviewed.[72] This change in the reporting rate was significant enough to raise the odds ratio from a non-statistically-significant figure prior to 2014 to a statistically significant figure afterward.[73] The authors of the study, including

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70 (*See, e.g.*, Berge et al., *Genital use of talc and risk of ovarian cancer: a meta-analysis*, 27(3) Eur J Cancer Prev. 248, 253 (2018) ("Berge 2018") (attached as Ex. A11 to Tersigni Cert.); Terry et al., *Genital Powder Use and Risk of Ovarian Cancer: A Pooled Analysis of 8,525 Cases and 9,859 Controls*, 6(8) Cancer Prevention Res. 811, 820 (2013) (attached as Ex. A139 to Tersigni Cert.); Langseth et al., *Perineal Use of Talc and Risk of Ovarian Cancer*, 62 J. Epidemiology & Cmty. Health 358, 358 (2008) (attached as Ex. A88 to Tersigni Cert.).)

71 (Pls.' Br. at 19.)

72 (General Causation Br. at 25.)

73 (*Id.*)

plaintiffs' expert Patricia Moorman, expressly noted "[t]he possibility of differential misclassification" (in other words, recall bias) "due to the heightened awareness of" talc-ovarian cancer litigation that resulted from media reports in 2014.[74]

While the Schildkraut study is persuasive evidence of the problem of recall bias in the case-control research, it simply is not true that Drs. Saenz and Holcomb dismissed all case-control studies based on it. To the contrary, Dr. Saenz testified that the Schildkraut study is just one "piece of data" that "show[s] the influence of recall bias in case-control studies,"[75] which she considered alongside other studies that also discuss and illustrate this problem.[76] Dr. Holcomb similarly referred to the Schildkraut study as simply "a good example of" recall bias,[77] and explicitly rejected plaintiffs' suggestion that his opinion that the case-control studies are subject to recall bias is based on that study alone.[78]

Nor is there any merit to plaintiffs' argument that the Schildkraut authors (including their own expert, Dr. Moorman) were "wrong" to "assum[e]" that media

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74 Schildkraut 2016 at 1416.

75 (Saenz Dep. 305:5-12.)

76 (*Id.* 305:20-306:3.)

77 (Holcomb Dep. 264:19-21.)

78 (*Id.* 268:9-15.)

coverage of talc litigation could have contributed to recall bias among participants in that study – and that none of the other studies plaintiffs' experts cite could have been affected by recall bias – because "[t]he first media coverage of any talcum powder litigation occurred in February 2016."[79] For one thing, there were "multiple news reports [regarding the alleged risks of talc] between 1982 and 2013" that could have contributed to recall bias in the case-control studies relied on by plaintiffs.[80] And in any event, recall bias is not limited to situations with substantial publicity. Rather, it is an inherent limitation of all case-control studies that are based on personal recollection.

Notably, both Dr. Saenz and Dr. Holcomb address sources of recall bias aside from media coverage in their expert reports. As Dr. Holcomb explains, a number of "factors have been shown to impact the level of accuracy or recall of an exposure," including "time since the exposure, the level of detail requested, personal characteristics such as educational level and socioeconomic status, and desirability of the recalled event/exposure."[81] Similarly, Dr. Saenz notes that "[p]eople who have had more time to perseverate and consider every detail and

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79 (Pls.' Br. at 21.)

80 (Expert Report of Gregory Diette, M.D., MHS at 20, Feb. 25, 2019 (attached as Ex. C18 to Tersigni Cert.).)

81 (Holcomb Rep. at 9.)

aspect of their lives that may have factored into how they developed a certain disease state, in this case ovarian cancer," may over-report exposure to a particular agent, especially if they are able to gather – for example, from the way questions are asked – that a study is interested in that agent.[82] This is a significant concern here because many of the talc studies did not blind the participants to the purpose of the study, potentially alerting them that talc use was of interest, even if they had not heard or read about the purported link in the news before the study.[83]

Plaintiffs' insistence that recent "studies" explain "why recall bias is not an issue" in talc research[84] is also baseless. Indeed, the only so-called "study" plaintiffs cite that actually addressed recall bias is not a study at all but their favorite regulatory document, a ***draft*** health assessment from a regulatory agency in Canada.[85] And that document merely states that recall bias "is unlikely to be an important source of bias" in talc studies,[86] relying entirely on an editorial that was published ***before*** the Schildkraut study, and, in any event, cites no scientific support for this proposition.

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82 (Saenz Rep. at 12.)

83 (General Causation Br. at 37.)

84 (Pls.' Br. at 21.)

85 (*Id.*)

86 (*Id.*)

In sum, Drs. Saenz and Holcomb properly considered the risk of recall bias – and other potential limitations of case-control studies – in opining that the totality of the scientific literature does not support a causal connection between ovarian cancer and talc use.

B. Dr. Saenz Properly Considered Strength Of Association.

Plaintiffs also argue that Dr. Saenz improperly "dismissed" case-control studies with a statistically significant association "simply because they have an odds ratio that is less than 2.0."[87] Once again, plaintiffs use the word "dismiss" inaccurately to convey the impression that Dr. Saenz's thorough analysis was unmethodical. As the deposition testimony cited by plaintiffs makes clear, Dr. Saenz would deem such studies to have a "weak statistical association, a weak odds ratio."[88] This does not in any way mean she "dismissed" them. It simply means she applied the exact methodology that is ***required*** in considering the first Bradford Hill factor: strength of association.

Notably, plaintiffs fail to cite ***any*** authority for the proposition that the scientific community considers an association in the range of 1.2 to 1.6 to be strong. By contrast, as set forth in detail in defendants' General Causation Brief,[89]

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87 (Pls.' Br. at 15.)

88 (Saenz Dep. 154:4-14 (quoted in Pls.' Br. at 15).)

89 (*See* General Causation Br. at 31-35.)

numerous scientific sources have deemed odds ratios in this range to be "weak."[90] Indeed, even plaintiffs' own experts were forced to concede as much at their depositions, noting that that an odds ratio in this range is "weak" or, at most, "modest."[91] And while plaintiffs argue that Dr. Saenz was unable to cite any

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[90] *See, e.g.*, Wynder et al., *Weak Associations in Epidemiology and Their Interpretation*, 11 Preventive Med. 464, 465 (1982) ("Wynder 1982") (attached as Ex. A157 to Tersigni Cert.) ("the term 'weak' refers to relative risks between 1.0 and 2.0"); Health Canada, Draft Screening Assessment: Talc ($Mg_3H_2(SiO_3)_4$) (Chem. Abstracts Serv. Registry No. 14807-96-6), at 21 (2018) (attached as Ex. A58 to Tersigni Cert.) ("small" association); Letter from Steven M. Musser, Ph.D., Deputy Dir. for Sci. Operations, Ctr. for Food Safety & Applied Nutrition, to Samuel S. Epstein, M.D., Cancer Prev. Coalition, Univ. of Ill. – Chi. School of Pub. Health, at 4 (Apr. 1, 2014) (attached as Ex. A89 to Tersigni Cert.) ("small positive associations"); Berge 2018 at 248 (abstract) ("weak" association). (*See also* Dep. of Anne McTiernan, M.D., Ph.D. 101:5-17, Jan. 28, 2019 (attached as Ex. B2 to Tersigni Cert.) (testifying that the World Cancer Research Fund concluded that "[e]ven if there were an increased risk, scientists estimate it would be small") (citation omitted).)

[91] (*E.g.*, Dep. of Arch I. Carson, M.D., Ph.D. ("Carson Dep.") 230:18-231:5, 232:13-233:23, Jan. 19, 2019 (attached as Ex. B5 to Tersigni Cert.) ("weak or modest"); Dep. of Sarah E. Kane, M.D. 256:24-257:4 (attached as Ex. B45 to Tersigni Cert.) (similar); Dep. of Sonal Singh, M.D., M.P.H. ("Singh Dep.") 140:19-25, Jan. 16, 2019 (attached as Ex. B47 to Tersigni Cert.) (similar).) Correspondingly, plaintiffs' experts have been unable to identify any scientific source characterizing a relative risk in the 1.2-1.6 range as probative of a strong association. (*E.g.*, Dep. of Daniel L. Clarke-Pearson, M.D. ("Clarke-Pearson Dep.") 130:10-15, Nov. 16, 2018 (attached as Ex. B10 to Tersigni Cert.) (failing to identify any peer-reviewed literature on talc and ovarian cancer that states 1.3 is a strong association); Dep. of Patricia G. Moorman, M.S.P.H., Ph.D. 251:9-13, Jan 25, 2019 (attached as Ex. B39 to Tersigni Cert.) (same); Singh Dep. 140:19-141:20 (same); Dep. of Ellen Blair Smith, M.D. 289:19-290:3, Jan. 9, 2019 (attached as Ex. B11 to Tersigni Cert.) (same).)

authority to support the notion that an odds ratio below 2.0 is weak,[92] this is a misrepresentation of her testimony. Dr. Saenz merely stated that she did not "off the top of [her] head have an epidemiological textbook" or other source "in [her] recollection" that she could cite to support the point while being questioned by plaintiffs' attorney.[93] This does not render her opinion unreliable. After all, the reliability of an expert's methods is assessed based on the relevant scientific literature, not on her recall of it at any particular time.[94] *See, e.g., In re C. R. Bard, Inc., Pelvic Repair Sys. Prods. Liab. Litig.*, MDL No. 2187, 2018 WL 4220602, at *4 (S.D. W. Va. Sept. 5, 2018) (denying motion to exclude expert testimony on ground that the expert was unable to identify specific literature supporting his opinions during his deposition because he had amply "substantiated his opinion with testable, peer-reviewed literature" generally). As discussed above, Dr. Saenz's analysis of the strength factor of the Bradford Hill analysis – i.e., her assessment that the association of 1.2 to 1.6 identified in certain case-control

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92 (*See* Pls.' Br. at 15 (citing Saenz Dep. 155:23-156:5).)

93 (Saenz Dep. 155:23-156:5.)

94 Indeed, plaintiffs' counsel assured defense witnesses that their depositions were not intended to be memory tests. (*See, e.g.*, Dep. of Ie-Ming Shih, M.D., Ph.D. 11:7-9, Mar. 26, 2019 (attached as Ex. B28 to Tersigni Cert.) (assuring Dr. Shih, at the beginning of the deposition, that "[t]oday is not going to be a memory test," and that if he "need[ed] to review documents, it's open book").)

studies is "weak" – is well-supported by the scientific literature. For this reason, too, plaintiffs' attacks on her epidemiology opinions fail.

C. Dr. Holcomb Properly Considered Statistical Significance.

Plaintiffs also repeat their now-familiar attack on statistical significance, arguing that Dr. Holcomb's opinions are unreliable because he "conveniently dismissed" studies with results that are not statistically significant as irrelevant to assessing causation.[95] This argument misconstrues Dr. Holcomb's position, despite his repeated attempts to clarify at his deposition that he did ***not*** categorically claim that a study had to be statistically significant to have any relevance to a causation analysis.[96] It is also wrong as a matter of science and the law.

As Dr. Holcomb explained in his deposition testimony, a study with an odds ratio of 1.09 and a confidence interval of 0.86 to 1.37 does not show an elevated risk because "the true risk estimate is somewhere between having a . . . 14 percent

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95 (Pls.' Br. at 16.)

96 Dr. Holcomb disputed this characterization at least twice in his testimony, and after each instance, plaintiffs' counsel quickly moved on. (*See* Holcomb Dep. 199:10-18 ("Q. Doctor, have you cited any authority to support your claims that studies that don't show statistical significance are attributable to chance and bias? A. No. That's not -- that's not my claim, first of all. Q. Okay. Doctor, do you know who Sander Greenland is?"); *id.* 241:20-242:8 ("Q. Is it your opinion that unless a given study is statistically significant and with an odds ratio greater than or equal to 2.0, that the findings are attributable to random chance? A. No. Q. That's not your opinion? A. No. Q. Who is Melissa Frey?").)

reduction in risk to a 37 percent increase in risk."[97] Thus, he noted, it would misunderstand statistics to find a positive association any time the odds ratio is greater than one without regard to whether the finding reached a statistically significant level.[98]

Plaintiffs do not contradict these assertions. Instead, they offer the nonsensical argument that Dr. Holcomb's lack of familiarity with Drs. Rothman and Greenland – two epidemiologists who have taken an outlier position that statistical significance should be ignored – somehow proves that he "lacks knowledge and understanding of the statistical science" generally.[99] But the fact that a few courts have cited a textbook written by these authors does not mean that it is the "seminal" textbook on epidemiology, or that anyone who "disagree[s] with" Drs. Rothman and Greenland with respect to the importance of statistical significance may not reliably provide expert testimony on the subject.[100] To the contrary, as explained in detail in the J&J defendants' Omnibus *Daubert* Opposition Brief, Rothman and Greenland have taken a controversial position with

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97 (Holcomb Dep. 348:18-16.)

98 (*See id.* 193:14-194:10.)

99 (Pls.' Br. at 17.)

100 (*Id.*)

respect to statistical significance that is contrary to the approach embraced by the scientific community.[101]

Plaintiffs also argue that Dr. Holcomb admitted that he "is unable to cite any support for" the position that a study's odds ratio must be "statistically significant" to be relevant to causation.[102] This argument is similarly meritless. In truth, Dr. Holcomb explained at his deposition that the importance of scientific significance "is so widely accepted" by the scientific community "that it would be like finding an authority that says water is H_2O."[103] Perhaps for this reason, and as discussed in more detail in defendants' Omnibus *Daubert* Opposition Brief, the Third Circuit (and other courts) have made clear that experts are not free to ignore whether study results are statistically significant in forming causation opinions. *See In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 793-94, 799 (3d Cir. 2017); *see also Bracco Diagnostics, Inc. v. Amersham Health, Inc.*, 627 F. Supp. 2d 384, 452 (D.N.J. 2009) (Wolfson, J.) (excluding opinions of an expert who "testified that the 0.05 p-value test for statistical significance was not grounded in solid science"; such statements were "not properly based upon

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101 (*See* Defs.' Mem. of Law in Resp. to Pls.' Steering Committee's Omnibus Br. Regarding *Daubert* Legal Standard & Scientific Principles for Assessing General Causation ("Omnibus *Daubert* Opp'n Br.") at 15-19 (filed herewith and incorporated herein).)

102 (Pls.' Br. at 16-17.)

103 (Holcomb Dep. 195:13-196:15.)

science and [were] not reliable"); *In re Lipitor (Atorvastatin Calcium) Mktg., Sales Practices & Prods. Liab. Litig.*, 892 F.3d 624, 642 (4th Cir. 2018) (affirming exclusion of Dr. Sonal Singh – also an expert for plaintiffs here – "because the plaintiffs 'failed to demonstrate that Dr. Singh's reliance on non-statistically significant "trends" is accepted in his field, that non-statistically significant findings have served as the basis for any epidemiologist's causation opinion in peer-reviewed literature, or that standards exist for controlling the technique's operation'") (citation omitted).

For all of these reasons, plaintiffs' attacks on the causation opinions offered by Drs. Holcomb and Saenz are baseless and should be rejected.[104]

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[104] Plaintiffs' suggestion that the opinions of Drs. Saenz and Holcomb are somehow deficient because their respective reports did not include a separate "methodology" section (Pls.' Br. at 7) is also baseless. Courts have recognized that, as long as the methodology employed by an expert is clear from his or her opinions and testimony, it need not be "explicitly state[d]" in the expert report. *Glenn v. Procter & Gamble Co.*, No. 07-4144-EFM, 2009 WL 10688943, at *5 n.31 (D. Kan. Sept. 10, 2009) (expert opinion admitted "[e]ven though [the expert] did not explicitly state in his expert report the methodology he used to come to this conclusion" because it was "clear . . . based on his report and deposition testimony, that he followed [a particular, recognized] methodology"). Here, both Drs. Saenz and Holcomb testified that they applied the well-established Bradford Hill framework in evaluating causation, and explained how they did so. (*See* Saenz Dep. 184:2-16, 186:23-188:16, 190:10-191:20; Holcomb Dep. 159:22-160:6, 163:24-165:3, 172:19-22.) In addition, both experts reference the Bradford Hill criteria in their reports, addressing, among other things, strength of association, consistency of association, dose response, biological plausibility and analogy. (*See* Saenz Rep. at 8-30; Holcomb Rep. at 19-23.)

II. DRS. SAENZ AND HOLCOMB PROPERLY REJECTED PLAINTIFFS' EXPERTS' BIOLOGICAL PLAUSIBILITY OPINIONS AS UNSUPPORTED BY RELIABLE SCIENTIFIC EVIDENCE.

Plaintiffs next argue that Drs. Saenz and Holcomb imposed an improper "heightened burden of proof" and failed to consider the totality of the evidence in concluding that there is no biologically plausible method by which talc can cause ovarian cancer.[105] This argument is premised on a misrepresentation of the opinions of Drs. Saenz and Holcomb, a misunderstanding of biological plausibility, and a misinterpretation of the law governing experts' choice of literature. Drs. Saenz and Holcomb properly rejected plaintiffs' experts' biological plausibility hypotheses as unsupported by reliable scientific evidence, and properly considered a wide variety of studies and other evidence in doing so.

A. Drs. Saenz And Holcomb Properly Analyzed Biological Plausibility.

Plaintiffs argue that Drs. Saenz and Holcomb's biological plausibility opinions should be excluded because they supposedly rest on an incorrect standard – i.e., that plaintiffs must provide concrete "proof" of a biological mechanism as opposed to establishing what is biologically plausible.[106] But it is clear from context that neither witness testified that biological plausibility means a proven

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105 (Pls.' Br. at 22-31.)

106 (*Id*. at 22.)

mechanism; rather, they both testified – consistent with the opinions set forth in their reports – that some "***evidence***" of a mechanism is required.

For example, although Dr. Saenz used the word "proof" in testifying about biological plausibility, she was not using that term in any legal sense; rather, it is clear from her testimony that when she said "there has to be some ***proof***," she simply meant there has to be some ***evidence***. Indeed, Dr. Saenz explained just that a few lines later in her testimony:

> My understanding is that there has to be biologic evidence that what you're hypothesizing could actually happen. It doesn't have to be that you have to prove that talc itself could migrate, but there's no studies of any migration whatsoever in the human that any particulate matter applied to the perineum can make it all the way to the ovaries.[107]

This testimony fully comports with Dr. Saenz's report, which makes clear that "[a] scientist cannot just say that because a hypothesis makes theoretical sense, it is so. Instead, scientific data are needed to support the contention, and . . . no data" support the theory being proffered.[108]

Plaintiffs also emphasize Dr. Holcomb's testimony that migration is "not a proven point" and that his "bar is a little higher,"[109] but a closer reading of that testimony similarly demonstrates that Dr. Holcomb (like Dr. Saenz) was describing

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107 (Saenz Dep. 198:11-18 (emphasis added).)

108 (Saenz Rep. at 30.)

109 (Pls.' Br. at 23.)

biological plausibility in terms of the lack of supportive evidence rather than definitive proof. Indeed, the highlighted testimony was part of Dr. Holcomb's critique of the conclusions of a 2018 unpublished manuscript by Mohamed Taher, which itself acknowledges that "[d]ata on talc migration in the genital tract of animals is inconsistent" and concludes that chronic inflammation is merely a "possible mechanism[]."[110] As Dr. Holcomb explained, without scientific evidence demonstrating that talc can migrate from the human perineum to the ovaries, the statement in Taher regarding biological plausibility is rank "conjecture" by the authors and does not support plaintiffs' experts' theory of biological plausibility.[111] And such testimony is likewise consistent with the opinion set forth in Dr. Holcomb's report that the "studies examining" plaintiffs' proposed biological mechanism "do not support" their theory.[112]

In short, the testimony cited by plaintiffs does not suggest that Drs. Saenz or Holcomb imposed a "heightened burden" or an "incorrect standard" for biological plausibility, much less that they "insist[ed] on certainty or near certainty."[113]

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110 Taher et al., *Systematic Review and Meta-Analysis of the Association Between Perineal Use of Talc and Risk of Ovarian Cancer* 24, 26 (2018) (unpublished manuscript) (attached as Ex. A137 to Tersigni Cert.).

111 (Holcomb Dep. 445:16-24; *see also id*. 422:15-17, 423:8-424:3.)

112 (Holcomb Rep. at 21.)

113 (Pls.' Br. at 22, 30-31.)

Rather, Drs. Saenz and Holcomb merely explain that the opinions of plaintiffs' experts are nothing more than bare "hypothes[es]" that are not supported by scientific data demonstrating that particulate matter applied to the perineum can travel to the ovaries and fallopian tubes.[114] These are reliable opinions that apply the proper standard for biological plausibility.

B. Drs. Saenz And Holcomb Were Not Required To Review Every Study That Is Remotely Related To Biological Plausibility.

Plaintiffs also argue that the opinions of Drs. Saenz and Holcomb are unreliable because they did not read a handful of studies that plaintiffs claim are

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[114] (*See* Saenz Dep. 197:6-13, 198:11-13; Holcomb Dep. 422:6-17.) Plaintiffs also make the preposterous claim that Drs. Saenz and Holcomb actually conceded that there is a biologically plausible mechanism by which perineally applied talc can migrate to the fallopian tubes and ovaries (*see* Pls.' Br. at 26-27), despite their repeated and unequivocal assertions to the contrary (*see, e.g.*, Saenz Rep. at 22, 27-31; Saenz Dep. 198:11-18, 233: 21-25; Holcomb Rep. at 3, 22; Holcomb Dep. 422:7-17). Again, this argument is directly refuted by the record. While Dr. Saenz testified that "there is some data that there can be particulate matter that can make it to the ovaries" (Saenz Dep. 209:10-12 (quoted in Pls.' Br. at 26-27)), it is clear from context that she was referring only to a particular 1961 study by Egli & Newton, which did ***not*** involve talc (*id.* 209:9-210:7) and employed specific "conditions that were optimal for rapid transport" of the inserted particles, Egli & Newton, *The Transport of Carbon Particles in the Human Female Reproductive Tract*, 12 Fertility & Sterility 151, 152 (1961) (attached as Ex. A31 to Tersigni Cert.). Similarly, while Dr. Holcomb testified that it is "possible" that talc could migrate from the perineum to the ovaries (Holcomb Dep. 421:23-422:15 (quoted in Pls.' Br. at 27)), he clearly did not view that mere possibility as plausible (*id.* 422:11-17). Indeed, Dr. Holcomb testified that he is not aware of a single study showing that talc applied perineally migrated to a woman's ovaries or fallopian tubes. (*Id.* 438:24-439:4.)

inconsistent with the experts' positions on biological plausibility.[115] This argument is similarly without merit.

As set forth in the J&J defendants' Omnibus *Daubert* Opposition Brief, "[n]othing in *Daubert* . . . requires an expert to consider every single article on a topic in order to be admitted as an expert." *In re C. R. Bard, Inc., Pelvic Repair Sys. Prods. Liab. Litig.*, MDL No. 2187, 2018 WL 4220616, at *5 (S.D. W. Va. Sept. 5, 2018) (expert's alleged failure to consider a "handful of articles" was not unreliable).[116] As such, plaintiffs' allegation that Drs. Saenz and Holcomb did not read a few studies does not establish that their testimony is unreliable.

This is all the more true because the articles that plaintiffs claim Drs. Saenz and Holcomb should have read are irrelevant to these experts' analyses and do not in any way undermine their opinions, as confirmed by their deposition testimony. For instance:

- Dr. Saenz stressed that the Buz'Zard & Lau 2007 study does not even "demonstrate cancer" – much less a causal relationship between talc and ovarian cancer in particular.[117] Rather, it tested an immortalized granulosa cell line that is only possibly relevant to sex cord-stromal

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115 (*See* Pls.' Br. at 27-29.)

116 (*See* Omnibus *Daubert* Opp'n Br. at 9-10 (citing cases).)

117 (Saenz Dep. 259:3-8.) Notably, when Dr. Holcomb attempted to "explain" why the Buz'Zard study does not support plaintiffs' theory of biological plausibility, plaintiffs' counsel would not even allow him to do so and cut him off on the ground that counsel "didn't ask [him] for an explanation." (Holcomb Dep. 166:7-167:6.)

tumors (which can arise from granulosa tissues, and which several plaintiffs' experts do not even allege can be caused by talc).[118] In any event, the study did not identify "malignant transformation from a normal cell," which, as Dr. Saenz has explained, would be necessary for the study to support a plausible mechanism by which talc causes ovarian cancer.[119]

- Dr. Saenz explained that the Sjosten 2004 paper involved vaginal application of cornstarch rather than perineal application of talcum powder.[120]

- Kunz 1997 involved the placement of particles (albumin spheres, used as a proxy for sperm) directly into the reproductive tract,[121] and accordingly fails to show that peristaltic contractions can aid the upward migration of perineally applied talc. Dr. Holcomb testified that the study does not "mean that talc is able to retrograde translocate" and criticized plaintiffs' experts for "cit[ing] studies that don't prove . . . the point that they're trying to make" regarding biological plausibility.[122]

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[118] *See* Buz'Zard & Lau, *Pycnogenol reduces Talc-induced Neoplastic Transformation in Human Ovarian Cancer Cultures*, 21 Phytotherapy Res. 579, 580 (2007) (attached as Ex. A16 to Tersigni Cert.). (*See also, e.g.*, McTiernan Rep. at 17 (stating that "[o]nly epithelial ovarian cancer has been studied in relation to use of talcum powder products" and therefore that her report is referring to "'epithelial ovarian cancer'" wherever it uses the term "'ovarian cancer,'" thereby excluding sex cord-stromal tumors from the scope of her opinions).)

[119] (Saenz Dep. 259:24-260:5.)

[120] (*Id*. 211:7-11.)

[121] *See* Kunz et al., *The Uterine Peristaltic Pump: Normal and Impeded Sperm Transport within the Female Genital Tract, in The Fate of the Male Germ Cell* 267, 270 (Ivell & Holstein eds. 1997) (attached as Ex. A86 to Tersigni Cert.).

[122] (Holcomb Dep. 438:4-11.) Plaintiffs' argument is all the more frivolous given that they did not even bother to question Dr. Saenz about the Kunz study. *In re C. R. Bard, Inc., Pelvic Repair Sys. Prods. Liab. Litig.*, MDL No. 2187, 2018 WL 4219563, at *3 (S.D. W. Va. Sept. 5, 2018) ("I decline to exclude Dr. Giudice solely for failing to comment on specific articles never presented to him for

- Dr. Saenz testified that the Shukla 2009 paper did not involve "malignant transformation."[123] Rather, it addressed gene expression – which does not by itself say anything about the ostensible carcinogenicity of talc – and focused largely on mesothelial cells and asbestos.[124] To the limited extent the study addressed talc and ovarian cells, it showed no effect on gene expression.[125]

- Dr. Saed's made-for-litigation 2019 paper was not even published at the time Drs. Saenz and Holcomb issued their reports. In any event, Dr. Saed summarized his 2019 paper in his expert report, which Drs. Saenz and Holcomb both reviewed.[126] Moreover, Dr. Holcomb read the 2019 paper upon its being published and concluded that it does ***not*** support the plausibility of plaintiffs' hypothetical biological mechanism for multiple reasons.[127]

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comment."; "nothing in *Daubert* requires an expert to consider every single article on a topic in order to be admitted as an expert").

[123] (Saenz Dep. 178:20-25.)

[124] *See* Shukla et al., *Alterations in Gene Expression in Human Mesothelial Cells Correlate with Mineral Pathogenicity*, 41 Am. J. Respiratory Cell Mol Biol. 114 (2009) (attached as Ex. A131 to Tersigni Cert.). (*See also* Expert Report of Michael Birrer, M.D., Ph.D. ("Birrer Rep.") at 16, Mar. 29, 2019 (attached as Ex. C33 to Tersigni Cert.).)

[125] (*See* Birrer Rep. at 16.) As one of the study's authors, defense expert Dr. Mossman, explained at her deposition, the experiment did not "attempt[] to show changes with talc carcinogenicity"; talc was simply used as a control. (Dep. of Brooke T. Mossman, M.S., Ph.D. 362:14-16, Apr. 8, 2019 (attached as Ex. B7 to Tersigni Cert.).)

[126] (*See* Saenz Dep. 98:2-5 ("I've not read the publication from 2019. I have read his expert report wherein he describes the experiments he did, I believe, for that publication.").)

[127] (Holcomb Dep. 433:1-435:21.) Plaintiffs also fault Drs. Saenz and Holcomb for failing to read the Zervomanolakis 2007 paper (*see* Pls.' Br. at 28); however, in that study, particles were inserted at the posterior fornix – well into the vaginal tract, *see* Zervomanolakis et al., *Physiology of Upward Transport in the Human Female Genital Tract*, 1101 Ann. N.Y. Acad. Sci. 1, 3, 7 fig.1, 10 (2007) (attached

In light of this testimony, there is no basis to contend that Drs. Saenz and Holcomb unreliably excluded any literature from their review. *In re Horizon Organic Milk Plus DHA Omega-3 Mktg. & Sales Practice Litig.*, No. 12-MD-02324, 2014 WL 1669930, at *8 (S.D. Fla. Apr. 28, 2014) ("While the defendant is correct that an expert may not 'cherry pick' the available data in order to manufacture a desired result, Dr. Bazinet has provided a reasonable, scientific explanation why he relied on some studies . . . and discounted other studies.").[128] For this reason, too, plaintiffs' arguments should be rejected.

III. DR. SAENZ IS QUALIFIED TO CRITICIZE DR. SMITH-BINDMAN, AND HER CRITICISMS ARE RELIABLE.

Finally, plaintiffs ask the Court to exclude Dr. Saenz's criticisms of Dr. Smith-Bindman's epidemiological review on the asserted grounds that: (1) Dr. Saenz is not qualified to offer them; and (2) Dr. Saenz's criticisms are "misguided" and "based on *ipse dixit*."[129] These arguments, too, are meritless.

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as Ex. A159 to Tersigni Cert.) – making it irrelevant to plaintiffs' migration theory here.

[128] (*See also* Defs.' Mem. of Law in Supp. of Mot. to Exclude Pls.' Experts' Ops. Related to Biological Plausibility at 16-17, 26-30, 58-60, May 7, 2019 (ECF No. 9736-1).)

[129] (Pls.' Br. at 32.)

First, plaintiffs argue that Dr. Saenz "lacks the basic qualifications to critique Dr. Smith-Bindman's epidemiological assessment" because she "is not an epidemiologist and does not have any degrees in epidemiology."[130] Courts have repeatedly held, however, that physicians with relevant clinical and research expertise do not need a degree in epidemiology to be qualified to opine on epidemiological research. *See In re Mirena IUD Prods. Liab. Litig.*, 169 F. Supp. 3d 396, 426 (S.D.N.Y. 2016) (holding that gynecologic oncologists were qualified to opine regarding epidemiology because "medical doctors do not need to be epidemiologists in order to testify regarding epidemiological studies"); *Wolfe v. McNeil-PPC, Inc.*, 881 F. Supp. 2d 650, 659 (E.D. Pa. 2012) ("Even if Dr. Salisbury does not have the particular degree or training that might be 'most appropriate' to interpret epidemiological literature, his extensive medical training and experience are sufficient."); *In re Avandia Mktg., Sales Practices & Prods. Liab. Litig.*, No. 2007-MD-1871, 2011 WL 13576, at *10 (E.D. Pa. Jan. 4, 2011) (rejecting the argument that a cardiologist was not qualified to "analyze and draw conclusions from epidemiological research" where the expert had "credentials as a researcher and published author, as well as clinician" and "his ability to analyze the epidemiological research" was "demonstrated in his report"); *accord Pineda v. Ford Motor Co.*, 520 F.3d 237, 244 (3d Cir. 2008) (explaining that the Third

130 (*Id.*)

Circuit "interpret[s] Rule 702's qualification requirement liberally," recognizing that a "broad range of knowledge, skills, and training qualify an expert") (citation omitted).[131]

Dr. Saenz is more than qualified to opine on the topic of epidemiology under this standard. As set forth above, Dr. Saenz is a board-certified gynecological oncologist who teaches "fellows, residents and medical students about all aspects of gynecologic malignancies, ***including their epidemiology***."[132] As she explained at her deposition, although she is not "formally trained in epidemiology, [she has] published epidemiologic literature and [has] certainly review[ed] epidemiologic literature on a ***regular*** basis as [it] pertains to gynecologic oncology."[133] Such extensive experience with epidemiology actually exceeds that of many of plaintiffs' own experts who (despite not being epidemiologists "by training") nonetheless claim to be sufficiently qualified to weigh in on the epidemiological

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131 Plaintiffs' cases are completely irrelevant. (Pls.' Br. at 32 (citing *Calhoun v. Yamaha Motor Corp., U.S.A.*, 350 F.3d 316, 322 (3d Cir. 2003) (considering expert qualifications to opine on the design of a jet ski); *Elcock v. Kmart Corp.*, 233 F.3d 734, 741 (3d Cir. 2000) (considering expert qualifications to opine on vocational rehabilitation)).)

132 (Saenz Rep. at 1 (emphases added).)

133 (Saenz Dep. 129:14-17.)

data.[134] In short, plaintiffs are pressing a double standard on qualifications (as they do in their other *Daubert* briefs) that should be rejected by the Court.

Second, plaintiffs also argue that Dr. Saenz's identification of various "alleged errors" in Dr. Smith-Bindman's report related to case-control data are unreliable "*ipse dixit*."[135] The crux of plaintiffs' argument is that Dr. Saenz supposedly did not realize that Dr. Smith-Bindman was focusing on data regarding "daily [talc] use, or as close to daily use as possible" when identifying instances of inaccurate data reporting.[136] Although Dr. Saenz identified numerous such instances, plaintiffs argue that Dr. Smith-Bindman's focus on "daily use" made her data "consistent with those" from the underlying studies she examined.[137]

This unduly narrow criticism of Dr. Saenz's analysis is outright wrong. Most notably, Dr. Smith-Bindman's report explicitly states that she was ***not*** reporting data on "daily use" in the section of her report that Dr. Saenz addresses –

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134 (Dep. of Laura Plunkett, Ph.D., D.A.B.T. 356:3-7, Dec. 19, 2018 (attached as Ex. B33 to Tersigni Cert.); Carson Dep. 61:17-19.)

135 (Pls.' Br. at 32, 33-35.) Plaintiffs are wrong that "[m]ost of Dr. Saenz's review of the case-control studies" is a criticism of Dr. Smith-Bindman. (*See id.* at 32.) To the contrary, "most of" Dr. Saenz's discussion addresses limitations in the talc case-control studies that exist independently of Dr. Smith-Bindman's flawed analysis of them. (*See* Saenz Rep. at 9-13.)

136 (Pls.' Br. at 33.)

137 (*See id.* at 33-34.)

i.e., Table 4 of Dr. Smith-Bindman's report.[138] Although Dr. Smith-Bindman purports to have limited her analysis to "daily use" (or her subjective approximation of it)[139] in a different section of her report, Table 4 explicitly provides data on the "effect size for '***any exposure*** to talc.'"[140] To the extent Dr. Smith-Bindman's unpronounced intention was only to include "daily use" data in this table, Dr. Saenz could not have been expected to know that based on the express "any exposure" description that Dr. Smith-Bindman provided.

In any event, plaintiffs do not even attempt to defend the numerous data inaccuracies that exist in Dr. Smith-Bindman's report regardless of whether she was addressing "daily use" or "any use." Among these are the fact that none of the confidence intervals Dr. Smith-Bindman reported in the section of her report focusing on "daily use" match those reported in the original studies.[141] Tellingly,

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138 (Saenz Rep. at 9 ("Although she states that Table 4 in her report lists the OR as reported in the individual case-control studies for any genital exposure to talc, a careful check of the data in her table reveals that this is not the case.").)

139 (*See* General Causation Br. at 101-03 (explaining in detail that Dr. Smith-Bindman's definition of "daily use" was subjective and unreliable for a number of reasons).)

140 (Expert Report of Rebecca Smith-Bindman, M.D. at 19, Nov. 15, 2019 (attached as Ex. C36 to Tersigni Cert.) (emphasis added); *see also id.* at 30-34 (different section of Smith-Bindman's report purporting to "summarize results for regular users of talcum powder").)

141 (*See* General Causation Br. at 104-05; Dep. of Rebecca Smith-Bindman, M.D. Vol. I 182:13-183:24, Feb. 7, 2019 (attached as Ex. B40 to Tersigni Cert.).) Dr. Smith-Bindman was not even aware of these errors until confronted with them

plaintiffs identify only one example from Table 4 where the data from a study would have been accurate if limited to "daily use."[142] By contrast, many of the figures reported in Dr. Smith-Bindman's Table 4 do not correspond to ***any*** figures reported in the studies themselves – whether for "ever" or "never" use, daily use, or anything else.[143]

All of these criticisms of Dr. Smith-Bindman are elaborated in Dr. Saenz's report, which even includes a table comparing the data Smith-Bindman used to

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at her deposition, and she was only able to attempt to explain them on the second day of her deposition after inappropriately calling the statistician to whom she had delegated her data abstraction in between deposition sessions. (*See* Dep. of Rebecca Smith-Bindman, M.D. Vol. II 254:9-17, Feb. 8, 2019 (attached as Ex. B42 to Tersigni Cert.).) Her explanation – that the statistician had estimated rather than used the reported data (*id.* 256:6-13) – only shows that Dr. Saenz was correct to observe that data inaccuracies in Dr. Smith-Bindman's report raise serious questions about the reliability of her methodology.

[142] (*See* Pls.' Br. at 34 (arguing only that Dr. Smith-Bindman used accurate daily use data from Schildkraut 2016).)

[143] For example, the reported ORs and CIs for the following studies, among others, do not correspond to figures in the studies themselves: "Godard 1998" (Godard et al,. *Risk Factors for Familial and Sporadic Ovarian Cancer Among French Canadians: A Case-Control Study*, 179 Am. J. of Obstetrics & Gynecology 403 (1998) (attached as Ex. A164 to Suppl. Tersigni Cert.)); "Wong 1999" (Wong et al., *Perineal Talc Exposure and Subsequent Epithelial Ovarian Cancer: A Case-Control Study*, 93 Obstetrics & Gynecology 372 (1999) (attached as Ex. A176 to Suppl. Tersigni Cert.)); "Moorman 2009" (Moorman et al., *Ovarian Cancer Risk Factors in African-American and White Women*, 170 Am. J. of Epidemiology 598 (2009) (attached as Ex. A95 to Tersigni Cert.)); and "Rosenblatt 2011" (Rosenblatt et al., *Genital Powder Exposure and the Risk of Epithelial Ovarian Cancer*, 22 Cancer Causes & Control 737 (2011) (attached as Ex. A125 to Tersigni Cert.)).

those actually contained in the studies at issue.[144] Because Dr. Saenz supports her critiques with specific data, which is the opposite of "*ipse dixit*," plaintiffs' argument fails, and plaintiffs' motion should be rejected for this reason as well.

CONCLUSION

For the foregoing reasons, the Court should deny plaintiffs' motion to exclude the opinions offered by Drs. Saenz and Holcomb.

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Respectfully submitted,

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[144] (Saenz Rep. at 43, tbl. 1.)